

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 11 OCT 2000

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FEB 08 2001

Applicant's or agent's file reference N 1931-1 WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/SE99/01075	International filing date (day/month/year) 16.06.1999	Priority date (day/month/year) 22.06.1998
International Patent Classification (IPC) or national classification and IPC C07C 279/12, C07C 275/28, C07D 295/135, A61K 51/00, A61K 49/00, A61K 31/17, A61K 31/40		
Applicant AstraZeneca AB et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 18.01.2000	Date of completion of this report 18.09.2000
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 08-667 72 88	Authorized officer Gerd Strandell/GH Telephone No. 08-782 25 00

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/SE99/01075

I. Basis of the report

1. This report has been drawn on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*:

- ☒ the international application as originally filed.
- ☐ the description, pages _____, as originally filed,
 pages _____, filed with the demand,
 pages _____, filed with the letter of _____,
 pages _____, filed with the letter of _____.
- ☐ the claims, Nos. _____, as originally filed,
 Nos. _____, as amended under Article 19,
 Nos. _____, filed with the demand,
 Nos. _____, filed with the letter of _____,
 Nos. _____, filed with the letter of _____.
- ☐ the drawings, ~~sheets~~/fig _____, as originally filed,
~~sheets~~/fig _____, filed with the demand
~~sheets~~/fig _____, filed with the letter of _____,
~~sheets~~/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, ~~sheets~~/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/SE99/01075

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 15, 20-22

because:

☒ the said international application, or the said claims Nos. 15, 20-22

relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/SE99/01075

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	<u>2-14, 16-19</u>	YES
	Claims	<u>1</u>	NO
Inventive step (IS)	Claims	<u>11, 12</u>	YES
	Claims	<u>1-10, 13, 14, 16-19</u>	NO
Industrial applicability (IA)	Claims	<u>1-14, 16-19</u>	YES
	Claims	<u></u>	NO

2. Citations and explanations

The claimed invention relates to novel 1,4-substituted phenyl compounds of the general formula (I), a process for their preparation, pharmaceutical compositions comprising the novel compounds and their use in therapy, in particular in the management of pain.

The following relevant documents are cited:

- A) WO 9639382 A1 (FUJISAWA PHARMACEUTICAL CO., LTD.), 12 December 1996 (12.12.96)
- B) EP 0507291 A1 (YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD.), 7 October 1992 (07.10.92), page 12, line 23, the claims
- C) WO 9737646 A1 (BRISTOL-MYERS SQUIBB COMPANY), 16 October 1997 (16.10.97), page 31, line 6 -line 11

Document A) discloses compounds of a general formula, which embraces compounds of claim 1 of the present application or are structurally close to the compounds according to claims 2-5. The compounds have pharmacological activities and are inter alia useful for treatment of disorders associated with spinal trauma. Thus, claim 1 is not considered to be novel. Claims 2-10, 13, 14 and 16-19, are not considered to show inventive step as what is mentioned there seems to be obvious practical measures for a person skilled in the art. The applicant has not shown that the claimed compounds are likely to have any unexpected beneficial effects compared to those in the cited document.

.../...

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: V

Document B) discloses therapeutically useful compounds, which are structurally close to the compounds claimed in claims 1-5 of the present application. Thus, claims 1-6, 18 and 19 are not considered to show inventive step.

Document C) discloses a compound, which is structurally close to the compounds claimed in claims 1-5 of the present application. The compound is an intermediate for preparing therapeutically useful compounds.

Consequently, the invention claimed in claim 1 is not considered to fulfil the requirements of novelty and inventive step, but is considered to fulfil the requirement of industrial applicability. The invention claimed in claims 2-14 and 16-19 is considered to fulfil the requirements of novelty and industrial applicability. The invention claimed in claims 11 and 12 is considered to fulfil the requirement of inventive step, but the invention claimed in claims 2-10, 13, 14 and 16-19 is not considered to fulfil the requirement of inventive step.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO9852558	26.11.1998	21.05.1998	23.05.1997

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)
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16CS

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

ASTRAZENECA AB
Global Intellectual Property
Patents
S-151 85 Södertälje
SUÈDE

RECEIVED

DEC 08 2000

TECH CENTER 1600/2900

Date of mailing (day/month/year) 28 July 2000 (28.07.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference N 1931-1 WO	
International application No. PCT/SE99/01075	International filing date (day/month/year) 16 June 1999 (16.06.99)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address ASTRA AKTIEBOLAG S-151 85 Södertälje Sweden	State of Nationality SE	State of Residence SE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input checked="" type="checkbox"/> the name	<input type="checkbox"/> the address
<input type="checkbox"/> the nationality		
<input type="checkbox"/> the residence		
Name and Address ASTRAZENECA AB S-151 85 Södertälje Sweden	State of Nationality SE	State of Residence SE
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

From the INTERNATIONAL BUREAU

PCT

**NOTIFICATION OF THE RECORDING
OF A CHANGE**

(PCT Rule 92bis.1 and
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To:

ASTRAZENECA AB
Global Intellectual Property
Patents
S-151 85 Södertälje
SUÈDE

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NOV 27 2000

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Date of mailing (day/month/year)

28 July 2000 (28.07.00)

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N 1931-1 WO

International application No.

PCT/SE99/01075

International filing date (day/month/year)

16 June 1999 (16.06.99)

IMPORTANT NOTIFICATION

1. The following indications appeared on record concerning:

☐

the applicant

☐

the inventor

☒

the agent

☐

the common representative

Name and Address

ASTRA AKTIEBOLAG
Intellectual Property, Patents
S-151 85 Södertälje
Sweden

State of Nationality

State of Residence

Telephone No.

+46 8 553 260 00

Facsimile No.

+46 8 553 288 20

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐

the person

☒

the name

☒

the address

☐

the nationality

☐

the residence

Name and Address

ASTRAZENECA AB
Global Intellectual Property
Patents
S-151 85 Södertälje
Sweden

State of Nationality

State of Residence

Telephone No.

+46 8 553 260 00

Facsimile No.

+46 8 553 288 20

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒

the receiving Office

☐

the International Searching Authority

☒

the International Preliminary Examining Authority

☐

the designated Offices concerned

☒

the elected Offices concerned

☐

other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Beate Giffo-Schmitt

Telephone No.: (41-22) 338.83.38

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

ASTRAZENECA AB
Global Intellectual Property
Patents
S-151 85 Södertälje
SUÈDE

Date of mailing (day/month/year) 28 July 2000 (28.07.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference N 1931-1 WO	
International application No. PCT/SE99/01075	International filing date (day/month/year) 16 June 1999 (16.06.99)

1. The following indications appeared on record concerning:

☒ the applicant

 ☐ the inventor

 ☐ the agent

 ☐ the common representative

Name and Address

ASTRA PHARMA INC.
1004 Middlegate Road
Mississauga, Ontario L4Y 1M4
Canada

State of Nationality

CA

State of Residence

CA

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person

 ☒ the name

 ☐ the address

 ☐ the nationality

 ☐ the residence

Name and Address

ASTRAZENECA CANADA INC.
1004 Middlegate Road
Mississauga, Ontario L4Y 1M4
Canada

State of Nationality

CA

State of Residence

CA

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

After the change of name as specified above, the applicant has now assigned all rights to ASTRAZENECA AB and shall therefore be deleted from the records. ASTRAZENECA AB shall now be recorded as applicant for all designated States except the United States of America.

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Lombettes 1211 Genève 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Beate Giffo-Schmitt Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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NOTIFICATION OF THE RECORDING
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Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

ASTRA AKTIEBOLAG
Intellectual Property, Patents
S-151 85 Södertälje
SUÈDE

Date of mailing (day/month/year) 21 March 2000 (21.03.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference N 1931-1 WO	
International application No. PCT/SE99/01075	International filing date (day/month/year) 16 June 1999 (16.06.99)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent
<input type="checkbox"/> the common representative		
Name and Address ROBERTS, Edward Astra Research Centre Montreal 7171 Fredrick-Banting St Laurent, Quebec H4S 1Z9 Canada	State of Nationality GB	State of Residence CA
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address
<input type="checkbox"/> the nationality		
<input checked="" type="checkbox"/> the residence		
Name and Address ROBERTS, Edward Bruderholz Allee 174 CH-4059 Basel Switzerland	State of Nationality GB	State of Residence CH
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

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NOTIFICATION OF THE RECORDING
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From the INTERNATIONAL BUREAU

To:

ASTRA AKTIEBOLAG
Intellectual Property, Patents
S-151 85 Södertälje
SUÈDE

Date of mailing (day/month/year) 21 March 2000 (21.03.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference N 1931-1 WO	
International application No. PCT/SE99/01075	International filing date (day/month/year) 16 June 1999 (16.06.99)

1. The following indications appeared on record concerning:

☒ the applicant ☒ the inventor ☐ the agent ☐ the common representative

Name and Address

GREGOR, Vlad
Alanex Corp.
3550 General Atomics Court
San Diego, CA 92121
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address

GREGOR, Vlad
12283 Carmel Vista Road
219
San Diego, CA 92130
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☒ the International Preliminary Examining Authority ☐ other:
The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Beate Giffo-Schmitt

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 21 March 2000 (21.03.00)	
International application No. PCT/SE99/01075	Applicant's or agent's file reference N 1931-1 WO
International filing date (day/month/year) 16 June 1999 (16.06.99)	Priority date (day/month/year) 22 June 1998 (22.06.98)
Applicant DELORME, Daniel et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

18 January 2000 (18.01.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Beate Giffo-Schmitt

Telephone No.: (41-22) 338.83.38